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Regulatory network analysis of Epstein-Barr virus identifies functional modules and hub genes involved in infectious mononucleosis

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Abstract

© 2017 Springer-Verlag WienEpstein-Barr virus (EBV) is the most common cause of infectious mononucleosis (IM) and establishes lifetime infection associated with a variety of cancers and autoimmune diseases. The aim of this study was to develop an integrative gene regulatory network (GRN) approach and overlying gene expression data to identify the representative subnetworks for IM and EBV latent infection (LI). After identifying differentially expressed genes (DEGs) in both IM and LI gene expression profiles, functional annotations were applied using gene ontology (GO) and BiNGO tools, and construction of GRNs, topological analysis and identification of modules were carried out using several plugins of Cytoscape. In parallel, a human-EBV GRN was generated using the Hu-Vir database for further analyses. Our analysis revealed that the majority of DEGs in both IM and LI were involved in cell-cycle and DNA repair processes. However, these genes showed a significant negative correlation in the IM and LI states. Furthermore, cyclin-dependent kinase 2 (CDK2) – a hub gene with the highest centrality score – appeared to be the key player in cell cycle regulation in IM disease. The most significant functional modules in the IM and LI states were involved in the regulation of the cell cycle and apoptosis, respectively. Human-EBV network analysis revealed several direct targets of EBV proteins during IM disease. Our study provides an important first report on the response to IM/LI EBV infection in humans. An important aspect of our data was the upregulation of genes associated with cell cycle progression and proliferation.

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